

Research report

Frontal midline theta rhythm is correlated with cardiac autonomic activities during the performance of an attention demanding meditation procedure

Yasutaka Kubota^{a,*}, Wataru Sato^b, Motomi Toichi^c, Toshiya Murai^a, Takashi Okada^a, Akiko Hayashi^a, Akira Sengoku^a

^aDepartment of Neuropsychiatry, Faculty of Medicine, Kyoto University, Shogoin-Kawaharacho, Kyoto 606-8507, Japan

^bDepartment of Cognitive Psychology in Education, Kyoto University, Kyoto, Japan

^cDivision of Child and Adolescent Psychiatry, Case Western Reserve University/University Hospitals of Cleveland, Cleveland, OH, USA

Accepted 14 December 2000

Abstract

Frontal midline theta rhythm (Fm theta), recognized as distinct theta activity on EEG in the frontal midline area, reflects mental concentration as well as meditative state or relief from anxiety. Attentional network in anterior frontal lobes including anterior cingulate cortex is suspected to be the generator of this activity, and the regulative function of the frontal neural network over autonomic nervous system (ANS) during cognitive process is suggested. However no studies have examined peripheral autonomic activities during Fm theta induction, and interaction of central and peripheral mechanism associated with Fm theta remains unclear. In the present study, a standard procedure of Zen meditation requiring sustained attention and breath control was employed as the task to provoke Fm theta, and simultaneous EEG and ECG recordings were performed. For the subjects in which Fm theta activities were provoked (six men, six women, 48% of the total subjects), peripheral autonomic activities were evaluated during the appearance of Fm theta as well as during control periods. Successive inter-beat intervals were measured from the ECG, and a recently developed method of analysis by Toichi et al. (J. Auton. Nerv. Syst. 62 (1997) 79–84) based on heart rate variability was used to assess cardiac sympathetic and parasympathetic functions separately. Both sympathetic and parasympathetic indices were increased during the appearance of Fm theta compared with control periods. Theta band activities in the frontal area were correlated negatively with sympathetic activation. The results suggest a close relationship between cardiac autonomic function and activity of medial frontal neural circuitry. © 2001 Elsevier Science B.V. All rights reserved.

Theme: Neural basis of behavior

Topic: Learning and memory: physiology

Keywords: EEG; Frontal midline theta activity; Mental concentration; Anterior cingulate cortex; Cardiac autonomic function; Heart rate variability

1. Introduction

Since Hans Berger [2] reported a decrease in the amplitude of the alpha rhythm during the performance of mental arithmetic, it has been shown that task-related modulation of the ongoing EEG reflects changes in the state of the functional networks underlying task performance [3,33,36]. The alpha rhythm tends to decrease in

strength as tasks become more difficult [18–20,22,56]. In contrast, high-amplitude theta rhythm over the frontal lobes was noted to appear during mental tasks, and many studies have shown that the frontal midline theta rhythm (Fm theta) is related to attentive states that occur both during mental task performance and meditative concentration [5,17–20,22,24–27,35,42,51,54,55,66, for review, see 23].

Gevins et al. [17], reporting the increase of Fm theta rhythm during working memory tasks, localized the signal source to the anterior cingulate cortex (ACC) using dipolar models, and other topographic studies, including MEG

*Corresponding author. Tel.: +81-75-751-3383; fax: +81-75-751-3246.

E-mail address: yka@pluto.dti.ne.jp (Y. Kubota).

studies [1,28], also produced results consistent with their findings. Lesion studies of the ACC in humans revealed attentional deficits [9,10,15,29,62] and recent neuroimaging studies revealed changes in ACC activation when subjects were required to sustain attention or to process representations in working memory [8,11,21,39–41,47,49,52,53,63, for review, see 48]. Based on these findings, it can be speculated that Fm theta reflects activation of attentional/working memory systems in prefrontal neural circuitry, including the ACC.

The human ACC is a region involved in both cognitive and affective processes [for review, see 7,16,34]. Animal studies showed that changes of heart rate and blood pressure were caused by electrical or chemical stimulation of the ACC [12,13,31,38]. Electrical stimulation of the human ACC was noted to induce autonomic changes [32,50], and also to elicit a 3–8 Hz EEG rhythm in frontomedial recordings [4,59]. Recently, it was suggested that ACC was differentiated into a dorsal cognitive division (ACCd) and a ventral affective division (ACAd) on the basis of cytoarchitecture and patterns of projections as well as function [for review, see 7,16,64]. The ACCd is a part attentional network, and maintains reciprocal interconnections with lateral prefrontal cortex, parietal cortex, and premotor and supplementary motor areas [16]. By contrast, the ACAd is connected to the amygdala, periaqueductal gray, nucleus accumbens, hypothalamus, anterior insula, hippocampus and orbitofrontal cortex, and has outflow to autonomic, visceromotor and endocrine systems [16]. In addition, ACC is frequently activated in functional imaging studies of cognitive or affective processes, and reciprocal suppression of ACAd during cognitive process and that of ACCd during affective process were reported [6,14,64]. Based on these findings, it can be safely hypothesized that the task-related frontal theta rhythms, which reflect the activity of the attentional network including ACC, might have interrelation with the peripheral autonomic activities.

Therefore, we wished to investigate the relationship between the theta signals over the anterior frontal lobes and the peripheral autonomic activities under certain states of concentration during consecutive mental tasks. It is also known that Fm theta activity is provoked when the subjects are relieved from anxiety [43,57,58]. Thus, we suspected that concentrated but at the same time relaxed mental state would optimally provoke Fm theta activities. In the present study, we used a unique meditative concentration task with a constant level of moderate mental effort, so as to provoke theta activity for a certain period during task performance. The task is called 'Su-soku', originally a standard procedure for Zen meditation, requiring sustained attention and breath control. The autonomic activity during the generation of Fm theta was compared with that under control conditions for the same subject. To evaluate the function of the autonomic nervous system (ANS), we used a recently developed heart rate variability

(HRV) analysis, which allows separate assessment of cardiac sympathetic and parasympathetic functions [60].

2. Materials and methods

2.1. Subjects

Twenty-five healthy young subjects (11 males and 14 females, aged 18–34 years, mean 23.1) were recruited from among undergraduate students. They were all free from cardiac, respiratory, and other diseases that would cause ANS dysfunction. No subject was medicated and none was a smoker or habitual drinker. Informed consent was obtained from all of them in written form after the experimental procedures had been fully explained.

2.2. Collection of data

EEG and ECG were recorded simultaneously under control and mental task conditions. EEGs were recorded from 19 electrodes in the International 10–20 System, and digitized EEG signals (sampling frequency: 200 Hz) were stored for offline analysis using an NEC digital encephalograph (SYNAFIT 5000). The electrodes in right hemisphere and Fz, Cz, Pz were referred to the right earlobe and electrodes in left hemisphere were referred to the left earlobe. This reference pattern is usually adopted in our laboratory in order to detect unpredictable electrical activity from either earlobe. As a result, any right- or left focused activities were not observed in all the subjects, and the subsequent analyses were performed based on this reference pattern. The ECG signal (Lead 1) was fed through an analog-to-digital converter into a microcomputer, and the inter-beat interval (IBI) was measured with an accuracy of 1 ms, triggered by the R wave.

2.3. Procedure

The subject, with arm and scalp electrodes attached, was seated in an armchair with his or her eyes open in a quiet, electrically shielded room.

2.3.1. Control condition

Subjects were instructed to breathe harmoniously to the cue-sounds of an electrical metronome for 2.5 min. The respiratory rhythm was fixed at the rate of 16/min for male and 18/min for female subjects.

2.3.2. Fm theta condition under the performance of 'Su-soku' task

Keeping their respiration rate as described above, the subjects performed the continuous serial addition of cue-sounds for 2.5 min. Namely, they counted each inspiratory and expiratory breath rhythmically. This procedure, called 'Su-soku', is a standard method for the initial stage of Zen

meditation. The ‘Su-soku’ task in the present study can be regarded as a kind of mental task requiring sustained attention: it required the subject to count serially up to about 300 at a relatively slow rate. Task performance might deteriorate because of inattention due to drowsiness, which was checked by asking the subjects the number they had counted. The respiration rate during the task was kept constant, which minimized the possibility of hyperventilation, which might have influenced both EEG and ANS function.

After recording under the control conditions, continuous recording was carried out during five successive trials of the ‘Su-soku’ task. This was repeated twice for each subject (ten trials in total). The criteria of Fm theta were; a train of rhythmic waves, observed at a frequency of 6–7 Hz, having a focal distribution with maximum around the frontal midline in the EEG [25,27]. Based on the criteria, subjects with Fm theta induction was selected on the condition that Fm theta was observed at least in one of total ten trials. This procedure led us to choose 12 (48%) of the total 25 subjects (six males and six females, with mean age of 24.3 years). In each subject, the trial (150 s) with Fm theta induction was chosen for subsequent data analysis. In nine subjects, Fm theta was observed during only one trial. In three subjects Fm theta appeared across more than one trial, so the trial with most frequent appearance of Fm theta was selected.

2.4. Data analysis

For the Fm theta condition, 100 successive IBIs (70–90 s), which corresponded to the period of recurrent Fm theta appearance, were selected for the evaluation of cardiac autonomic function (CAF). Within the same period, digitized signals of the EEG (sampling rate 200 Hz, band-pass 1.5–100 Hz) were sampled for epoch of 1.28 s, which was repeated until ten epochs without any artifacts were obtained. From the record under the resting condition, the data of the duration of 100 successive IBIs were selected for the evaluation of CAF. EEG signal sampling was also performed in the same way within the same period.

The appearance of theta rhythm in the Fz electrode was quantitatively evaluated using spectral analysis. Alpha rhythm in the O1 and O2 electrode was also evaluated so as to detect the decline of vigilance. EEG data were uploaded to a microcomputer and digitally filtered to 256 points per segment (1.28 s). The spectral densities of theta (4.0–8.0 Hz) and alpha (8.0–12.0 Hz) waves were calculated by using computer program for EEG mapping ‘ATALAS’ (Kissei Comtec). The following procedures of spectral analysis were performed by the software. First, a Hanning window was applied to each 256-point segment, and spectral density was calculated in amplitude (micro V) using fast Fourier transform (FFT). The amplitude of alpha component in O1 and that in O2 were averaged to provide the amplitude of occipital alpha component. The amplitude

of Fz-theta and occipital alpha component was averaged across ten segments to provide the final mean value of each spectral band.

The CAF was evaluated using a geometric method of analyzing HRV, which can assess sympathetic and parasympathetic function, separately, based on short-term measurement of IBI. Briefly, the sequence of IBI (IBI1, IBI2, ..., IBI_n) was transformed into a figure on a 2-dimensional plane by plotting IBI_{k+1} against IBI_k, and indices of CAF were calculated from the graphic components of the plot. The methods are described in detail elsewhere [60,61]. The indices obtained by this method, the cardiac vagal index (CVI) and the cardiac sympathetic index (CSI), indicate vagal and sympathetic function separately. These two indices were demonstrated to be more reliable than conventional measures, including spectral analysis.

3. Results

3.1. The change of the mean value of theta and alpha power

Compared to the control conditions, the mean value of theta power in the Fz electrode showed a remarkable increase under the Fm theta conditions ($t(11)=6.14$, $P<0.001$, paired t -test, two-tailed) (Fig. 1). This change reflected the appearance of a frontal midline theta rhythm during the ‘Su-soku’ task. Occipital alpha power did not show any significant difference under the control conditions compared to the Fm theta conditions ($t(11)=0.68$, not significant versus control, paired t -test, two-tailed). An

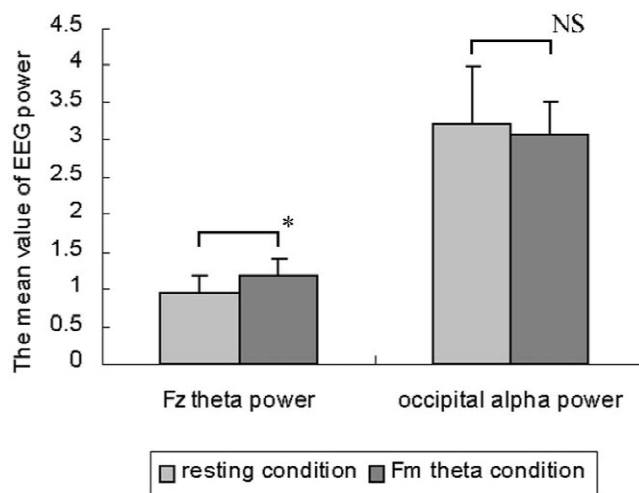


Fig. 1. Changes in the mean value of theta and alpha power (paired t -test, two-tailed; asterisk indicates $t(11)=6.14$, $P<0.001$; NS indicates $t=0.68$, not significant versus control. The standard deviation is illustrated).

example of EEG and topographical map at the appearance of Fm theta are shown (Fig. 2A,B).

3.2. The mean IBI

The mean IBI under the Fm theta conditions had a tendency to increase compared to that under the control conditions, from 886.3 ms (S.D. 33.0) to 924.0 ms (S.D. 47.6) ($t(11)=2.04$, $P=0.066$, not significant versus control, paired t -test, two-tailed).

3.3. The change of cardiac autonomic activities

Both CSI and CVI showed significant increases under the Fm theta conditions compared to control conditions (CSI: $t(11)=2.89$, $P<0.05$; CVI: $t(11)=6.39$, $P<0.001$, paired t -test, two-tailed) (Fig. 3).

3.4. The correlation of frontal theta activity with CSI and CVI

The change of CSI between the control conditions and the Fm theta conditions showed a negative correlation with

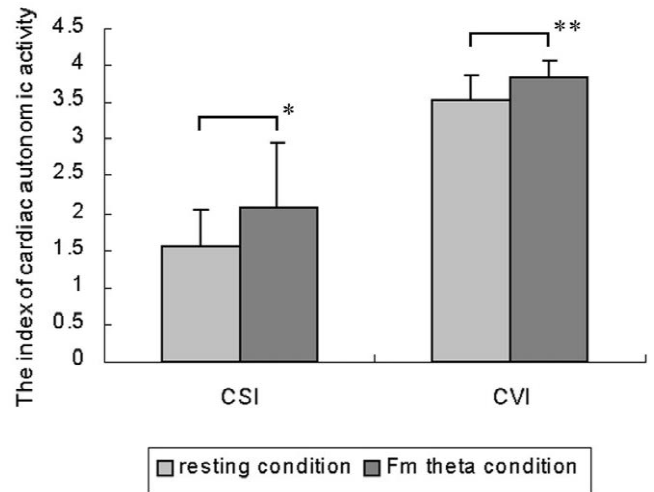


Fig. 3. Changes in cardiac sympathetic index (CSI) and cardiac vagal index (CVI) (paired t -test, two-tailed; asterisk indicates $t(11)=2.89$, $P<0.05$; double asterisk indicates $t(11)=6.39$, $P<0.001$. The standard deviation is illustrated).

the change of the mean value of theta power in Fz (correlation index: 0.72, $P<0.05$, Pearson's correlation coefficient test, two-tailed) (Fig. 4).

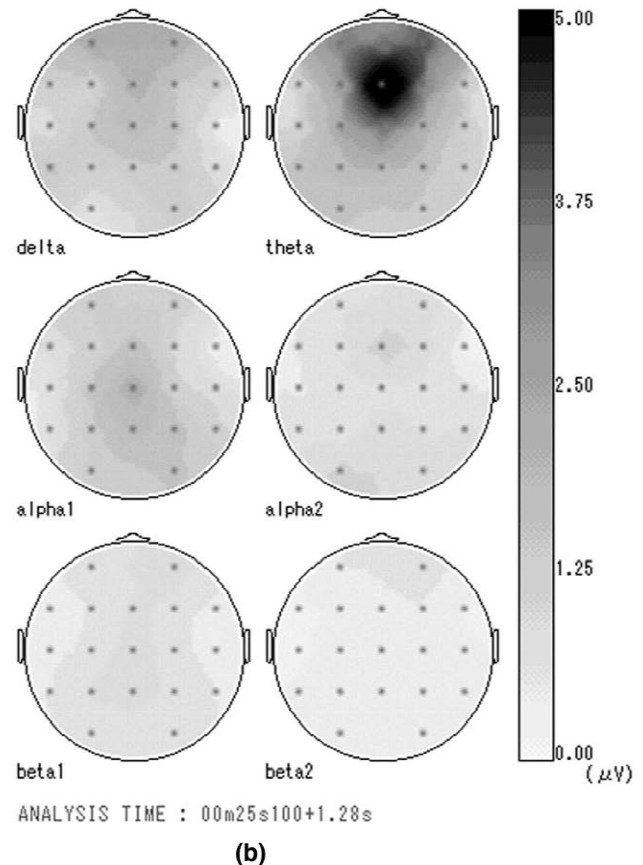
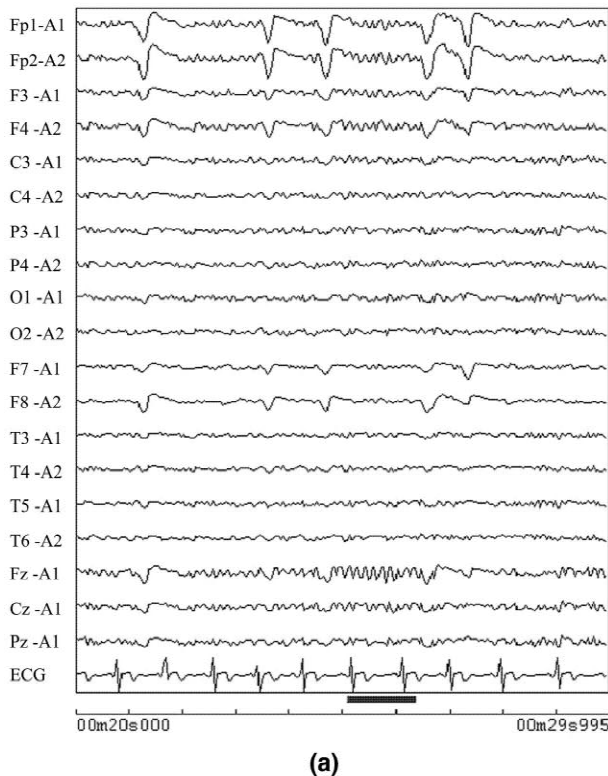


Fig. 2. (A) EEG sample taken from actual task period showing typical pattern of Fm theta. (B) EEG topographic map (from A) showing typical peak in theta band in Fz electrode. The spectral density of delta (1.0–4.0 Hz), theta (4.0–8.0 Hz), alpha1 (8.0–10.0 Hz), alpha2 (10.0–12.0 Hz), beta1 (12.0–14.0 Hz), and beta2 (14.0–16.0 Hz) waves for the period of 1.28 s were calculated in amplitude (micro V) using fast Fourier transform (FFT).

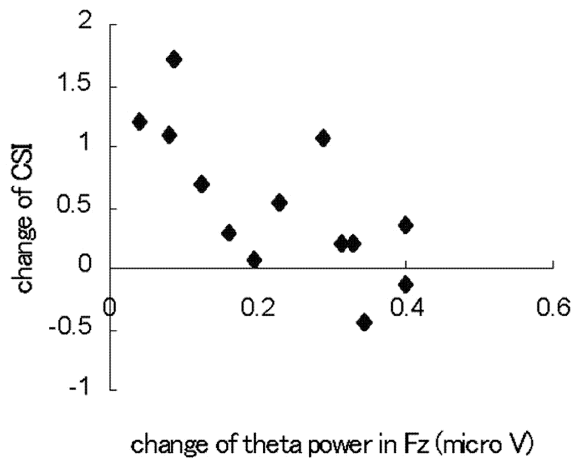


Fig. 4. Correlation between the change of the mean value of theta power in Fz and the change of CSI. Correlation index: 0.72 ($P < 0.05$, Pearson's correlation coefficient test, two-tailed).

4. Discussion

Theta signals over the mid-frontal area under the Fm theta conditions were reflected in the distinctive pattern in EEG topographic maps. The theta power was highest in Fz, and it showed a significant increase compared to that in the control state. The restricted distributions of theta signals distinguish them from the more topographically widespread slow rhythmic activity that has been associated with states of decreased alertness [30]. Occipital alpha activities did not show any difference between the Fm theta conditions and the control conditions, also indicating that the state with frontal theta waves can be distinguished from light drowsiness. EEG epochs suggesting a drowsy state, which is characterized by global slow activity, were found in some of our subjects. These epochs were easily distinguishable from the epochs with frontal theta waves in EEG topography, and in such cases the task performance was usually deteriorated.

The task used in the present study, 'Su-soku', can be regarded as a task requiring sustained attention. The task required the subject to count up to about 300 at a relatively slow rate, and does not need any special training to perform. In the case of subjects in the present study, Fm theta was provoked in 12 of the 25 subjects within the course of ten trials. Although the task is seemingly simple, the effort required to sustain attention appeared to be kept constant in the course of performance, and this effort to maintain a task-related attentional set might be responsible for the induction of Fm theta.

According to the debriefing of our subjects, they became immersed in the task of counting the numbers, and was also relaxed during the trial with Fm theta induction. Previous studies showed that mental task load decreased the mean IBI and increased the low frequency component of HRV, presumably due to sympathetic activation reflecting mental stress [37,44–46]. In contrast, our subjects with

frontal theta activity showed the tendency to increase mean IBI under the task load. This can be interpreted as indicating that with an appropriate level of mental concentration for task performance, bodily relaxation also occurs. This specific state at the periods of Fm theta appearance during task performance can be called 'relaxed concentration' [35].

The geometric method of analyzing HRV we introduced in the present study revealed the activity of the cardiac sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) during 'relaxed concentration'. The present study is, to our knowledge, the first study that evaluated the activity of the SNS and PNS separately under the attentive state during consecutive tasks. Both the SNS and PNS showed a certain level of tension for a relatively short period (70–90 s) marked by frontal theta activities. Co-activation of sympathetic and parasympathetic function during 'relaxed concentration' was related to the appearance of Fm theta in the cortical EEG, which appeared to reflect the functional correlates of frontal neural circuitry, including the ACC: that is, attentional/working memory systems and autonomic control in response to cognitive processes.

During the period of 'relaxed concentration' with Fm theta, CSI showed negative correlation with the mean value of theta power in Fz. The decrease of CSI can be interpreted in terms of the change of mental stress associated with task performance, which became smaller in the course of repeated trials. This tendency appeared to correlate with the changes in theta power that reflected the frontal neural activities during 'relaxed concentration'. Recent neuroimaging studies suggested different functioning of dorsal and ventral, i.e. 'cognitive' vs. 'affective' subdivisions of the ACC [7,16,64], and reciprocal suppression of the affective division of ACC during cognitive tasks was reported [6,14,65]. This is in accordance with the present result of negative correlation of frontal theta power with sympathetic activity during task performance.

In the case of CVI, any correlation with theta activities was not observed. As far as the present study is concerned, it is not clear why correlation was not observed regarding CVI. However, taking account of the fact that the cardiac parasympathetic activity changes rapidly compared to the cardiac sympathetic activity [44,67], there is a possibility that the lack of correlation with CVI might be due to the ceiling effect, that is, probably CVI reached easily the upper limit in great many part of our subjects during 'relaxed concentration' with Fm theta induction.

Although in the present study we did not determine the source of Fm theta, previous studies showed that the ACC is the source of Fm theta [1,17,28]. Those reports are in line with our hypothesis, taking account of the role of the ACC both in cognitive function and in autonomic control. On the other hand, other studies estimated the source of Fm theta to prefrontal area [26] or various part of the

dorsolateral frontal cortex in both hemispheres [51]. It should be noted that localization of sources is difficult using electrical techniques, and the results of these reports should be interpreted with a caution. There remains another possibility that Fm theta arises from other areas of frontal cortices such as the lateral prefrontal cortex (BA9) or the supplementary motor area. However, this issue is beyond a scope of the present study.

In summary, the present results indicated that theta band activities in the cortical EEG were closely related to cardiac autonomic function under the specific state during mental concentration, and there appeared to exist certain interactive relationships between the activities of peripheral autonomic activities and the frontal cortical network. Further studies are needed to investigate the neuroanatomical background of Fm theta, and we believe that Fm theta will cast light on the unknown neurophysiological mechanism underlying mind-body interaction in the cognitive process.

References

- [1] H. Asada, Y. Fukuda, S. Tsunoda, M. Yamaguchi, M. Tonoike, Frontal midline theta rhythms reflect alternative activation of prefrontal cortex and anterior cingulate cortex in humans, *Neurosci. Lett.* 274 (1999) 29–32.
- [2] H. Berger, Uber das Elektroenzephalogramm des Menschen, *Arch. Psychiatry (Nerven)* 87 (1929) 527–570.
- [3] E. Basar, C. Basar-Eroglu, S. Karakas, M. Schurmann, Brain oscillations in perception and memory, *Int. J. Psychophysiol.* 35 (2000) 95–124.
- [4] M.A. Brazier, Electrical activity recorded simultaneously from the scalp and deep structures of the human brain, *J. Nerv. Ment. Dis.* 147 (1968) 31–39.
- [5] N. Bruneau, S. Roux, P. Guerin, B. Garreau, G. Lelord, Auditory stimulus intensity responses and frontal midline theta rhythm, *Electroencephalogr. Clin. Neurophysiol.* 86 (1993) 213–216.
- [6] G. Bush, P.J. Whalen, B.R. Rosen, M.A. Jenike, S.C. McInerney, S.L. Rauch, The counting Stroop: an interference task specialized for functional neuroimaging — validation study with functional MRI, *Hum. Brain Mapp.* 6 (1998) 270–282.
- [7] G. Bush, P. Luu, M.I. Posner, Cognitive and emotional influences in anterior cingulate cortex, *Trends Cogn. Neurosci.* 4 (2000) 215–222.
- [8] S. Carlson, S. Martinkauppi, P. Rama, E. Salli, A. Korvenoja, H.J. Aronen, Distribution of cortical activation during visuospatial n-back tasks as revealed by functional magnetic resonance imaging, *Cereb. Cortex* 8 (1998) 743–752.
- [9] R.A. Cohen, R.F. Kaplan, D.J. Moser, M.A. Jenkins, H. Wilkinson, Impairments of attention after cingulotomy, *Neurology* 53 (1999) 819–824.
- [10] R.A. Cohen, R.F. Kaplan, P. Zuffante, D.J. Moser, M.A. Jenkins, S. Salloway, H. Wilkinson, Alteration of intention and self-initiated action associated with bilateral anterior cingulotomy, *J. Neuropsychiatry Clin. Neurosci.* 11 (1999) 444–453.
- [11] S.M. Courtney, L.G. Ungerleider, K. Keil, J.V. Haxby, Object and spatial visual working memory activate separate neural systems in human cortex, *Cereb. Cortex* 6 (1996) 39–49.
- [12] G.E. Crippa, V.L. Peres Polon, R.H. Kuboyama, F.M. Correa, Cardiovascular response to the injection of acetylcholine into the anterior cingulate region of the medial prefrontal cortex of un-anesthetized rats, *Cereb. Cortex* 9 (1999) 362–365.
- [13] G.E. Crippa, S.J. Lewis, A.K. Johnson, F.M. Correa, Medial prefrontal cortex acetylcholine injection-induced hypotension: the role of hindlimb vasodilation, *J. Auton. Nerv. Syst.* 79 (2000) 1–7.
- [14] H.D. Critchley, D.R. Corfield, M.P. Chandler, C.J. Mathias, R.J. Dolan, Cerebral correlates of autonomic cardiovascular arousal: a functional neuroimaging investigation in humans, *J. Physiol. (Lond.)* 523 (2000) 259–270.
- [15] A.R. Damasio, G.W. Van Hoesen, Emotional disturbances associated with focal lesions of the limbic frontal lobe, in: K.M. Heilman, P. Satz (Eds.), *Neuropsychology of Human Emotion*, Guilford Press, New York, 1983, pp. 85–110.
- [16] O. Devinsky, M.J. Morrell, B.A. Vogt, Contributions of anterior cingulate cortex to behaviour, *Brain* 118 (1995) 279–306.
- [17] A. Gevins, M.E. Smith, L. McEvoy, D. Yu, High-resolution EEG mapping of cortical activation related to working memory: effects of task difficulty, type of processing, and practice, *Cereb. Cortex* 7 (1997) 374–385.
- [18] A.S. Gevins, G.M. Zeitlin, J.C. Doyle, R.E. Schaffer, E. Callaway, EEG patterns during ‘cognitive’ tasks? Analysis of controlled tasks, *Electroencephalogr. Clin. Neurophysiol.* 47 (1979) 704–710.
- [19] A.S. Gevins, G.M. Zeitlin, J.C. Doyle, C.D. Yingling, R.E. Schaffer, E. Callaway, C.L. Yeager, EEG correlates of higher cortical functions, *Science* 203 (1979) 665–668.
- [20] A.S. Gevins, G.M. Zeitlin, J.C. Doyle, C.D. Yingling, M.F. Dedon, R.E. Schaffer, J.T. Roumasset, C.L. Yeager, EEG patterns during ‘cognitive’ tasks? Methodology and analysis of complex behaviors, *Electroencephalogr. Clin. Neurophysiol.* 47 (1979) 693–703.
- [21] D.R. Gitelman, A.C. Nobre, T.B. Parrish, K.S. LaBar, Y.H. Kim, J.R. Meyer, M. Mesulam, A large-scale distributed network for covert spatial attention: further anatomical delineation based on stringent behavioural and cognitive controls, *Brain* 122 (1999) 1093–1106.
- [22] A. Gundel, G.F. Wilson, Topographical changes in the ongoing EEG related to the difficulty of mental task, *Brain Topogr.* 5 (1992) 17–25.
- [23] K. Inanaga, Frontal midline theta rhythm and mental activity, *Psychiatry Clin. Neurosci.* 52 (1998) 555–566.
- [24] T. Inouye, K. Shinosaki, A. Iyama, Y. Matsumoto, S. Toi, Moving potential field of frontal midline theta activity during a mental task, *Cogn. Brain Res.* 2 (1994) 87–92.
- [25] T. Inouye, K. Shinosaki, A. Iyama, Y. Matsumoto, S. Toi, T. Ishihara, Potential flow of frontal midline theta activity during a mental task in the human electroencephalogram, *Neurosci. Lett.* 169 (1994) 145–148.
- [26] K. Iramina, S. Ueno, S. Matsuoka, MEG and EEG topography of frontal midline theta rhythm and source localization, *Brain Topogr.* 8 (1996) 329–331.
- [27] T. Ishihara, N. Yoshii, Multivariate analytic study of EEG and mental activity in juvenile delinquents, *Electroencephalogr. Clin. Neurophysiol.* 33 (1972) 71–80.
- [28] R. Ishii, K. Shinosaki, S. Ukai, T. Inouye, T. Ishihara, T. Yoshimine, N. Hirabuki, H. Asada, T. Kihara, S.E. Robinson, M. Takeda, Medial prefrontal cortex generates frontal midline theta rhythm, *NeuroReport* 10 (1999) 675–679.
- [29] K.W. Janer, J.V. Pardo, Deficits in selective attention following bilateral anterior cingulotomy, *J. Cogn. Neurosci.* 3 (1990) 231–241.
- [30] A. Jantani, S. Kidwai, W.J. Nowack, Episodic anterior drowsy theta in adults, *Clin. Electroencephalogr.* 17 (1986) 135–138.
- [31] B. Kaada, Somato-motor, autonomic and electrocorticographic responses to electrical stimulation of ‘rhinencephalic’ and other structures in primates, cat and dog, *Acta Physiol. Scand. Suppl.* 24 (1951) 1–285.
- [32] B. Kadda, H. Jasper, Respiratory responses to stimulation of temporal pole, insula, and hippocampal and limbic gyri in man, *Arch. Neurol. Psychiatry* 68 (1952) 609–619.

- [33] W. Kilmesh, Memory processes, brain oscillations and EEG synchronization, *Int. J. Psychophysiol.* 24 (1996) 61–100.
- [34] L. Koski, T. Paus, Functional connectivity of the anterior cingulate cortex within the human frontal lobe: a brain-mapping meta-analysis, *Exp. Brain Res.* 133 (2000) 55–65.
- [35] S.J. Laukka, T. Jarvilehto, Yu. Alexandrov, J. Lindqvist, Frontal midline theta related to learning in a simulated driving task, *Biol. Psychol.* 40 (1995) 313–320.
- [36] F. Lopes da Silva, Neural mechanisms underlying brain waves: from neural membranes to networks, *Electroencephalogr. Clin. Neurophysiol.* 79 (1991) 81–93.
- [37] D. Lucini, G. Covacci, R. Milani, G.S. Mela, A. Malliani, M. Pagani, A controlled study of the effects of mental relaxation on autonomic excitatory responses in healthy subjects, *Psychosom. Med.* 59 (1997) 541–552.
- [38] M. Maeda, S. Matsuura, K. Tanaka, J. Katsuyama, S. Nishimura, Effects of electrical stimulation on intracranial pressure and systemic arterial blood pressure in cats. Part II. Stimulation of cerebral cortex and hypothalamus, *Neurol. Res.* 10 (1988) 93–96.
- [39] J.A. Matochik, A.J. Zemetkin, R.M. Cohen, P. Hauser, B.D. Weintraub, Abnormalities in sustained attention and anterior cingulate metabolism in subjects with resistance to thyroid hormone, *Brain Res.* 723 (1996) 23–28.
- [40] G. McCarthy, A. Puce, R.T. Constable, J.H. Krystal, J.C. Gore, P. Goldman Rakic, Activation of human prefrontal cortex during spatial and nonspatial working memory tasks measured by functional MRI, *Cereb. Cortex* 6 (1996) 600–611.
- [41] A.R. McIntosh, Mapping cognition to the brain through neural interactions, *Memory* 7 (1999) 523–548.
- [42] Y. Miyata, Y. Tanaka, T. Hono, Long term observation on Fm-theta during mental effort, *Neuroscience* 16 (1990) 145–148.
- [43] Y. Mizuki, M. Suetsugi, I. Ushijima, M. Yamada, Differential effects of dopaminergic drugs on anxiety and arousal in healthy volunteers with high and low anxiety, *Prog. Neuropsychopharmacol. Biol. Psychiatry* 21 (1997) 573–590.
- [44] M. Pagani, R. Furlan, P. Pizzinelli, W. Crivellaro, S. Cerutti, A. Malliani, Spectral analysis of R–R and arterial pressure variabilities to assess sympatho-vagal interaction during mental stress in humans, *J. Hypertens. Suppl.* 7 (1989) S14–15.
- [45] M. Pagani, G. Mazzuero, A. Ferrari, D. Liberati, S. Cerutti, D. Vaitl, L. Tavazzi, A. Malliani, Sympathovagal interaction during mental stress. A study using spectral analysis of heart rate variability in healthy control subjects and patients with a prior myocardial infarction, *Circulation* 83 (Suppl. 4) (1991) II43–51.
- [46] M. Pagani, O. Rimoldi, P. Pizzinelli, R. Furlan, W. Crivellaro, D. Liberati, S. Cerutti, A. Malliani, Assessment of the neural control of the circulation during psychological stress, *J. Auton. Nerv. Syst.* 35 (1991) 33–41.
- [47] J.V. Pardo, P.J. Pardo, K.W. Janer, M.E. Raichle, The anterior cingulate cortex mediates processing selection in the Stroop attentional conflict paradigm, *Proc. Natl. Acad. Sci. USA* 87 (1990) 256–259.
- [48] T. Paus, L. Koski, Z. Caramanos, C. Westbury, Regional differences in the effects of task difficulty and motor output on blood flow response in the human anterior cingulate cortex: a review of 107 PET activation studies, *NeuroReport* 22 (1998) R37–R47.
- [49] K.M. Petersson, C. Elfgrén, M. Ingvar, Dynamic changes in the functional anatomy of the human brain during recall of abstract designs related to practice, *Neuropsychologia* 37 (1999) 567–587.
- [50] J. Pool, J. Ransohoff, Autonomic effects on stimulating rostral portion of cingulate gyri in man, *J. Neurophysiol.* 12 (1949) 385–392.
- [51] K. Sasaki, A. Nambu, T. Tsujimoto, R. Matsuzaki, S. Kyuhou, H. Gemba, Studies on integrative functions of the human frontal association cortex with MEG, *Cogn. Brain Res.* 5 (1996) 165–174.
- [52] E.E. Smith, J. Jonides, Working memory in humans: neuropsychological evidence, in: M. Gazzaniga (Ed.), *The Cognitive Neurosciences*, MIT Press, Cambridge, 1995, pp. 1009–1020.
- [53] E.E. Smith, J. Jonides, Storage and executive processes in the frontal lobes, *Science* 283 (1999) 1657–1661.
- [54] M.E. Smith, L.K. McEvoy, A. Gevins, Neurophysiological indices of strategy development and skill acquisition, *Cogn. Brain Res.* 7 (1999) 389–404.
- [55] C.J. Stam, Brain dynamics in theta and alpha frequency bands and working memory performance in humans, *Neurosci. Lett.* 286 (2000) 115–118.
- [56] M.B. Serman, C.A. Mann, D.A. Kaiser, B.Y. Suyenobu, Multiband topographic analysis of a simulated visuomotor aviation task, *Int. J. Psychophysiol.* 16 (1994) 49–56.
- [57] M. Suetsugi, Y. Mizuki, I. Ushijima, T. Kobayashi, K. Tsuchiya, T. Aoki, Y. Watanabe, Appearance of frontal midline theta activity in patients with generalized anxiety disorder, *Neuropsychobiology* 41 (2000) 108–112.
- [58] M. Suetsugi, Y. Mizuki, I. Ushijima, M. Yamada, J. Imaizumi, Anxiolytic effects of low-dose clomipramine in highly anxious healthy volunteers assessed by frontal midline theta activity, *Prog. Neuropsychopharmacol. Biol. Psychiatry* 22 (1998) 97–112.
- [59] J. Talarirach, J. Bancaud, S. Geier, M. Bordas-Ferrer, A. Bonis, L. Szikla, M. Rusu, The cingulate gyrus and human behavior, *Electroencephalogr. Clin. Neurophysiol.* 58 (1973) 519–524.
- [60] M. Toichi, T. Sugiura, T. Murai, A. Sengoku, A new method of assessing cardiac autonomic function and its comparison with spectral analysis and coefficient of variation of R-R interval, *J. Auton. Nerv. Syst.* 62 (1997) 79–84.
- [61] M. Toichi, Y. Kubota, T. Murai, Y. Kamio, M. Sakihama, T. Toriuchi, T. Inakuma, A. Sengoku, K. Miyoshi, The influence of psychotic states on the autonomic nervous system in schizophrenia, *Int. J. Psychophysiol.* 31 (1999) 147–154.
- [62] A.U. Turken, D. Swick, Response selection in the human anterior cingulate cortex, *Nat. Neurosci.* 2 (1999) 920–924.
- [63] R. Vandenberghe, J. Duncan, P. Dupont, R. Ward, J.B. Poline, G. Bormans, J. Michiels, L. Mortelmans, G.A. Orban, Attention to one or two features in left or right visual field: a positron emission tomography study, *J. Neurosci.* 17 (1997) 3739–3750.
- [64] B.A. Vogt, D.M. Finch, C.R. Olson, Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions, *Cereb. Cortex* 2 (1992) 435–443.
- [65] P.J. Whalen, G. Bush, R.J. McNally, S. Wilhelm, S.C. McInerney, M.A. Jenike, S.L. Rauch, The emotional counting Stroop paradigm: a functional magnetic resonance imaging probe of the anterior cingulate affective division, *Biol. Psychiatry* 44 (1998) 1219–1228.
- [66] S. Yamamoto, S. Matsuoka, Topographic EEG study of visual display terminal VDT performance with special reference to frontal midline theta waves, *Brain Topogr.* 2 (1990) 257–267.
- [67] Y. Yamamoto, R.L. Hughson, Coarse-graining spectral analysis: New method for studying heart rate variability, *J. Appl. Physiol.* 71 (1991) 1143–1150.